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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/813,640	03/21/2001	Kiichiro Yano	10287-071001/MGH 1585.1	2899

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EXAMINER

ANGELL, JON E

ART UNIT PAPER NUMBER

1635

DATE MAILED: 07/03/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/813,640

Applicant(s)

YANO ET AL.

Examiner

J. Eric Angell

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 08 April 2003.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-31 is/are pending in the application.
- 4a) Of the above claim(s) 1-28 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 29-31 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 21 March 2001 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 3.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_

### DETAILED ACTION

1. This Action is in response to the communication filed on 4/8/03, as Paper No. 9. Claims 1-31 are presently pending in the application and are addressed herein.

### *Election/Restrictions*

2. Applicant's election without traverse of Group IX (claims 29-31) in Paper No. 9 is acknowledged.
3. Claims 1-28 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 9, filed 4/8/03.
4. Claims 29-31 are examined herein.

### *Claim Rejections - 35 USC § 112, second paragraph*

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:  

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.
6. Claim 29 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: (1) providing a cell, and (2) treating the cell with the test compound. Without the missing steps it is unclear how one would evaluate the test compounds ability to modulate VEGF activity because it is not disclosed how one would evaluate VEGF activity in a cell-free system.

***Claim Rejections - 35 USC § 112, first paragraph***

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 29-31 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for:

A method for identifying compounds that modulate hair growth wherein said method comprises:

- (a) isolating vibrissa follicles,
- (b) treating said vibrissa follicles with a test compound, and
- (c) determining the level or activity of VEGF in the cells of said vibrissa follicles;

whereby a change in the level or activity of VEGF in the vibrissa follicle cells treated with said test compound relative to control cells indicates that said test compound may modulate hair growth;

does not reasonably provide enablement for the full scope encompassed by the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CA FC 1988).

*Wands* states on page 1404,

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“Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.”

The nature of the invention

The instant claims are drawn to a method for identifying a compound that modulates hair growth or hair thickness by identifying compounds that modulate VEGF level or activity.

The breadth of the claims

The presently pending claims are very broad and encompass in vitro as well as in vivo methods. Furthermore, the broadly claimed method suggests that any compound which modulates the level or activity of VEGF in any cell-type would indicate that the compound is a modulator of hair growth or hair thickness.

The unpredictability of the art and the state of the prior art

The relevant prior art recognizes that vascularization and blood supply is fundamental for hair growth. For instance, Kozłowska et al. (Arch. Dermatol. Res. 1998, Vol. 290, pages 661-668) teaches,

“An adequate supply of blood as a prerequisite for normal cell growth and differentiation seems to be of fundamental importance in the active processes of hair growth. The dermal papilla of the hair follicle as well as the bulge... present a well developed vascularization, thus providing optimal growth conditions.” (See p. 661, under “Introduction”); and,

“Hair follicle vascularization appears to be closely related to the processes involved in hair cycle regulation, in which growth factors, cytokines and other bioactive molecules are involved. In particular, vascular endothelial growth factor (VEGF), essential for

angiogenesis and vascular permeability, may be responsible for maintaining proper vasculature around the hair follicle during the anagen growth phase.” (See abstract).

Kozłowska indicates that it was the aim of their experiments to determine the expression and secretion of VEGF in the different cell types of the human hair follicles in order to determine which cell types could be involved in hair growth. The specific types of cells studied by Kozłowska were: dermal papilla cells, fibrous sheath fibroblasts, dermal fibroblasts, and follicular and interfollicular keratinocytes.

Based on the teachings of the prior art, one of skill in the art would recognize that VEGF expression could be associated with the regulation of hair growth; however, only when the VEGF expression is in the cells associated with the hair follicle (including perifollicular cells such as keratinocytes). That is, one of skill in the art would recognize that VEGF expression in cells associated with hair follicles might be important for hair growth, but would not recognize VEGF expression in other cells (i.e. cells not associated with hair follicles) as important for hair growth.

#### Working Examples and Guidance in the Specification

The specification discloses an example utilizing a mouse vibrissa organ culture system to assay the effect of VEGF on hair growth and hair thickness (see p. 21-22). In the working example, vibrissa follicles were isolated from mouse whicker pads. The hair length and shafts were measured in control follicles and VEGF-treated follicles. In the absence of a functional vascular system, VEGF did not affect hair growth, suggesting that the effects of VEGF are mediated through induction of perifollicular angiogenesis.

#### Quantity of Experimentation

The claims are very broad and encompass assaying the effect of the test compound on VEGF expression/activity in any cell-type. Considering that one of skill in the art would only recognize VEGF expression/activity in cells associated with the hair follicle as being important for hair growth, additional experimentation would be required to first establish that VEGF expression/activity in cells not associated with hair follicles could be involved in hair growth. Furthermore, the claims encompass in vitro as well as in vivo methods of assaying the test compounds effect on VEGF expression/activity. However, the specification only discloses the mouse vibrissa organ culture system (i.e., an in vitro method) to assay the effect of VEGF on hair growth and hair thickness. The specification does not disclose any in vivo methods for assaying the effect of a test compound on VEGF expression/activity.

#### Level of the skill in the art

The level of the skill in the art is deemed to be high.

#### Conclusion

Considering the nature of the invention, the breadth of the claims, the teaching of the prior art that cells other than hair follicle-associated cells would not likely be involved in hair growth, the limited number of working examples and guidance in the specification; and the high degree of skill required, it is concluded that the amount of experimentation required to perform the broadly claimed invention to the full scope encompassed by the claims is undue.

***Claim Rejections - 35 USC § 102***

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 29-31 are rejected under 35 U.S.C. 102(b) as being anticipated by Lachgar et al. (British Journal of Dermatology 1998, Vol. 138, pages 407-411).

The instant claims are drawn to a method of selecting a compound that modulates hair growth or hair thickness comprising providing a test compound, and evaluating the ability of the test compound to modulate VEGF activity wherein if the compound modulates VEGF activity it is selected as a compound that modulates hair growth (claim 29); wherein the test compound is applied to a cell, tissue or subject, and determining the level or expression of VEGF in the treated cell, tissue or subject compared to a control (claim 30); wherein the cell is a keratinocyte (claim 31).

Lachgar teaches a method wherein hair follicle dermal papilla (which controls hair growth and is par of the vibrissa follicle) is isolated in culture and a test compound (here, minoxidil) was administered to the cultured follicular dermal papilla and the expression of VEGF was assayed by measuring the VEGF mRNA level as well as VEGF protein level in the treated and untreated control cells (e.g., see abstract; p. 409, Fig. 1; p. 410, Figs. 2 and 4). Lachgar teaches, "The demonstration in this study that minoxidil can effect DPC-derived EGF protein and mRNA levels implies a critical role for minoxidil regulating DPC vascularization, and strongly supports the likely involvement of minoxidil in hair growth via a stimulation of VEGF production by DPC." Therefore, it is



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clear that Lachgar teaches a method of identifying compounds (such as minoxidil) that modulate hair growth by assaying the effect of the test compound on VEGF expression in cultured dermal papilla cells, including keratinocytes.

***Conclusion***


No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to J. Eric Angell whose telephone number is (703) 605-1165. The examiner can normally be reached on M-F (8:00-4:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader can be reached on (703) 308-0447. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

J. Eric Angell  
June 29, 2003



DAVE T. NGUYEN  
PRIMARY EXAMINER